REMARKS

This is in response to the Official Action of July 24, 2008.

New claims 15-16 is submitted herewith to complete the record. Claim 15 is supported by the specification by, among other things, originally presented and currently pending claims 8, 9, 10, and 11 (as sequentially renumbered). New claim 16 is likewise supported by originally presented claim 11 (as renumbered from 10 to 11). Entry and consideration thereof is respectfully requested.

The requirement for restriction having been made final, the claims of **Group I** (claims 1-7) are cancelled herein, without prejudice to the filing of a divisional application thereon.

The points raised in the Official Action are addressed below in the order originally set forth.

A. Claim objections.

Claim 8 stands objected to as containing language in the past tense. This claim has been rewritten in the present tense in the manner suggested in the action, and it is respectfully submitted that this rejection may now be withdrawn.

Claim 9 stands rejected as refering to Figure 1, it being noted that claims should stand alone to define the invention. Reconsideration is respectfully requested. It is common in mechanical and electrical patent practice for claims to contain reference numbers to elements illustrated in the Figures as an aid to construction thereof. In chemical and biological practice, it remains routine for claims to refer to Figures when the figure illustrates an element in a manner that would be cumbersome and unclear to articulate by words. Recent examples include, but are not limited to, US Patent No. 7, 386,398 (Issued June 10, 2008) where claim 1 reads, in pertinent part, as follows:

> 1. A method of identifying a compound that may bind to HCV NS5B, comprising the steps of: a) obtaining the structural coordinates of one of FIGS. 4 through 6; b) applying a 3-dimensional molecular modeling algorithm to the structural coordinates of an HCV NS5B binding pocket defined by the structural coordinates of at least amino acid residues 392, 393, 395, 396, 399, 424, 425, 428, 429, 492, 493, 494, 495, 500 and 503, and

> optionally one of: amino acid residues 37 and 496, of native HCV NS5B as ***shown in said Figure*** to determine the spatial coordinates of....

and US Patent No. 6,656,681 (issued December 2, 2003), where claim 1 reads, in pertinent part:

> 1. A method for screening a subject to determine whether said subject is a carrier of or is afflicted with a PKD1-associated disorder, which method comprises ... a nucleic acid comprising about 5.5 Kb flanked by the two Xbal sites ***shown in FIG. 3a*** and encompassing ... between the SM6 and JH17 fragment ***shown in FIG. 6***... to within fragment CW15 and 5' of the PKD1 gene to between fragments SM6 and JH17 ***as shown in FIG. 12***...

and US Patent No. 6,270,752 (issued August 7, 2001), where claim 1 reads:

> 1. Hydroalcoholic mixture of beta-pinene, camphene, beta-myrcene, limonene, cineole (1,8-epoxy-p -methane), camphor, linalol, bornyl acetate, isobornyl acetate, menthol, terpinen-ol, isoborneol monoterpens, ***having a chromatogram as shown in the Figure***.

and US Patent No. 5,814,613 (issued September 29, 1998), where claim 1 reads, in pertinent part:

> 1. A compound LL-E19020 Gamma comprising:...
> (e) a characteristic ultraviolet absorption spectrum ***as shown in FIG. I*** of the attached drawings;
> (f) a characteristic infrared absorption spectrum ***as shown in Figure II*** of the attached drawings;
> (g) a characteristic proton nuclear magnetic resonance spectrum ***as shown in Figure III*** of the attached drawings;
> (h) a characteristic carbon-13 nuclear magnetic resonance spectrum ***as shown in Figure IV*** of the attached drawings...,

Accordingly, reconsideration and withdrawal of the objection to claim 9 is respectfully requested.

B. Claim rejections—35 USC 102

Claims 8-9 and 12-13 stand rejected under 35 USC 102(b) over ***Moeller et al.*** To simplify the issues, claim 8 has been amended to incorporate claim 10, without prejudice or disclaimer. Accordingly, it is respectfully submitted that this rejection is now moot and should be withdrawn.

C. Claim rejections—35 USC 103.

Claims 8-13 stand rejected under 35 USC 103 as obvious over ***Moeller et al.*** in view of ***Larson et al.*** and further in view of ***Watanabe et al.*** It is alleged that, while Moeller et al. does not teach Iatrobeads, Larson et al. teach that Iatrobeads can be used to separate glycolipids, that Moeller states that *Pfiesteria piscicida* comprises a lipophilic portion, and Watanabe teach that solvents using a column packed with silica gel provides the advantage of being non-toxic. Applicants respectfully disagee with this analysis, and for the reasons set forth below, reconsideration is respectfully requested.

As stated in the "Examination Guidelines for Determining Obviousness under 35 U.S.C. 103 in View of the Supreme Court Decision in KSR International Co. v. Teleflex Inc." (72 Fed. Reg. 57526, October 10, 2007; *hereinafter* "the Examination Guidelines"), in *KSR* "the Supreme Court reaffirmed the familiar framework for determining obviousness as set forth in *Graham v. John Deere Co*...." (Examination Guidelines, Federal Register at page 57526). Hence, and as long established under that framework, to establish a *prima facie* case of obviousness, three requirements must be satisfied (M.P.E.P. § 2143). First, the prior art relied upon, must contain some suggestion or incentive that would have motivated the skilled artisan to modify a reference or to combine references. *In re Oetiker,* 24 U.S.P.Q.2d 1443, 1446 (Fed. Cir. 1992); *In re Fine,* 837 F.2d at 1074; *In re Skinner,* 2 U.S.P.Q.2d 1788, 1790 (Bd. Pat. App. & Int. 1986). Second, the proposed modification or combination of the prior art must have a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. *See Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1209, 18 U.S.P.Q.2d 1016, 1023 (Fed. Cir. 1991). Third, the prior art reference or combination of references must teach or suggest all of the limitations of the claims. *See In re Wilson* 424 F.2d 1382, 1385, 165 U.S.P.Q. 494, 496 (CCPA 1970) ("All words in a claim must be considered in judging the patentability of that claim against the prior art").

It is accepted that the chemical arts, particularly the pharmaceutical arts, and still more particularly the treatment of cancer, is less predictable than many other fields of inventive

endeavor. The invention at issue in *KSR* was an adjustable gas-pedal system – an invention in the mechanical arts. The mechanical arts are generally recognized as relatively predictable as compared with the biotechnology or chemical arts. Indeed, the Federal Circuit recently articulated concerns regarding the application of the *KSR* holding to the chemical arts:

> To the extent an art is unpredictable, as the chemical arts often are, *KSR*'s focus on these 'identified, predictable solutions' may present a difficult hurdle because potential solutions are less likely to be genuinely predictable.

Eisai Co. v. Dr. Reddy's Laboratories, July 21, 2008 --- F.3d ----, 2008 WL 2791884 (Fed. Cir. 2008) (*emphasis added*; copy enclosed). Likewise, potential solutions in the biotechnology arts are also unlikely "to be genuinely predictable."

In view of the decision in *KSR*, the USPTO issued the Examination Guidelines for examination of applications with respect to the nonobviousness requirement of 35 U.S.C. §103. The Examination Guidelines set out seven different "rationales" designated "A" to "G" for maintaining an obviousness rejection under *KSR*. Under all of these rationales and/or their factual underpinnings, the touchstones for obviousness are phrased in terms of "predictability" or "reasonable expectation of success" or both. Specifically, the seven rationales are, in relevant part (emphasis added):

> A. Combining Prior Art Elements According to Known Methods to Yield Predictable Results based on articulation of the following findings:
> (1) . . .
> (2) . . .
> (3) a finding that one of ordinary skill in the art would have recognized that the results of the combination were predictable; and
> (4) . . .
>
> B. Simple Substitution of One Known Element for Another to Obtain Predictable Results based on articulation of the following findings:
> (1) . . .
> (2) . . .
> (3) a finding that one of ordinary skill in the art could have substituted one known element for another and the results of the substitution would have been predictable;
>
> C. Use of Known Techniques to Improve Similar Devices (Method, or Product)

in the Same Way based on articulation of the following findings:

(1) . . .

(2) . . .

(3) a finding that one of ordinary skill in the art could have applied the known "improvement" technique in the same way to the "base" device (method, or product) and the results would have been predictable to one of ordinary skill in the art; and

(4) . . .

D. Applying a Known Technique to a Known Device (Method, or Product) Ready for Improvement to Yield Predictable Results based on articulation of the following findings:

(1) . . .

(2) . . .

(3) a finding that one of ordinary skill in the art would have recognized that applying the known technique would have yielded predictable results and resulted in an improved system; and

(4) . . .

E. "Obviousness to Try" – Choosing from a Finite Number of Identified, Predictable Solutions, With a Reasonable Expectation of Success based on articulation of the following findings:

(1) . . .

(2) a finding that there had been a finite number of identified, predictable potential solutions to the recognized need or problem;

(3) a finding that one of ordinary skill in the art could have pursued the known potential solutions with a reasonable expectation of success; and

(4) . . .

F. Known Work in One Field of Endeavor May Prompt Variations of it for Use in Either the Same Field or a Different One Based on Design Incentives or Other Market Forces if The Variations Would Have Been Predictable to One of Ordinary Skill in the Art.

(1) . . .

(2) . . .

(3) . . .

(4) a finding that one of ordinary skill in the art, in view of the identified design incentives or other market forces, could have implemented the claimed variation of the prior art, and the claimed variation would have been predictable to one of ordinary skill in the art; and

(5) . . .

G. Some Teaching, Suggestion, or Motivation in the Prior Art That Would Have Led One of Ordinary Skill to Modify the Prior Art Reference To Combine Prior Art Reference Teachings To Arrive at the Claimed Invention based on articulation of the following findings:

(1) . . .
(2) a finding that there was reasonable expectation of success; and
(3) . . .

Accordingly, to maintain an obviousness rejection under *KSR* (and the Examination Guidelines), the action must provide adequate reasoning regarding the predictability and reasonable expectation of success of the claimed invention by one of ordinary skill in the art in view of the prior art. In particular, the Examination Guidelines state that "[i]n short, the focus when making a determination of obviousness should be on what a person of ordinary skill in the art would have known at the time of the invention, and on what such a person would have been reasonably expected to have been able to do in view of that knowledge." (Federal Register at page 57527, top of third column; *emphasis added*). Further, the Examination Guidelines explain: "Note that combining known prior art elements is not sufficient to render the claimed invention obvious if the result should not have been predictable to one of ordinary skill in the art." (Federal Register at page 57529 (col. 3); *emphasis*).

Moeller et al. states, at the abstract thereof, as follows:

> We have developed chromatographic methodology to isolate a bioactive polar compound isolated from extracts of *Pfiesteria* culture and presently report the characterization of the activity of this substance. ***The molecular structural analysis of the polar active component(s) using mass spectrometry and nuclear magnetic resonance spectroscopy is currently under way.***

The cited reference further states, at page 743, as follows:

> The ***more polar (hydrophilic) fractions,*** derived from the SW extracts (F3, F4, and sometimes F5), contained a compound(s) that induced the GH4C1 reporter gene assay, demonstrated cytotoxicity in the GH4C1 assay, and killed both brine shrimp and fish. The F3 and F4 fractions obtained from the CM extracts of this strain induced the reporter gene assay, but only fraction F3 demonstrated any lethality to brine shrimp and occasionally fish. These fractions demonstrated activity in the GH4C1 cytotoxicity assay as well, although generally the responses were weak. We believe that the variability in

> assay response between CM and SW extracts could be due simply to a concentration effect, demonstrating that the active substance(s) is preferentially released from the cell rather than sequestered in any significant amounts. We believe that the polar fractions F3 and F4 from CM and SW probably represent the same compound or family of compounds. Preliminary LC-MS, NMR, and photo diode array-LC data (not shown) have yet to show any significant differences in the makeup of F3 and F4. This certainly d***oes not rule out distinct toxic substances in each***, however. Currently, ***large-scale mass culturing is under way to provide sufficient quantities of active fractions F3 and F4 for further chemical and structural analysis.***

Clearly the cited reference ***does not disclose a structure or clear characterization*** of the active compound (*e.g.*, in such detail as an NMR spectrum) and ***does not provide complete details of a method of making thereof.***

In the present case, no reasonable expectation of success is obtained because *Pfiesteria* toxin is foremost a water-soluble molecule, as specifically noted in the specification on page 1, in the first line of the *Background of the Invention* section. While Moeller may teach that this water soluble molecule contains a lipophilic portion, Moeller also recites that the compound is "a bioactive polar compound" and repeatedly refers to what is acknowledged therein as unidentified active compound as being "polar" and "water soluble". Hence, one would not be lead to a process that relies upon an apparently minor lipophilic portion of the as-yet unidentified active compound, as suggested in the Official Action, and—even if proposed—those skilled in the art would not have a reasonable expectation that such a process would be successful because the lipophilic portion of the active compound is apparently so minor that the compound is more frequently referred to as "polar" and "water soluble". Indeed, in the ***lead overview article*** in the same journal and volume of the cited reference, introducing the cited reference and other references in that volume, the identification of the *Pfiesteria* toxin is described as the requiring further research, as follows:

> ***Future research will undoubtedly focus on the isolation, purification, and characterization of the Pfiesteria toxin(s).*** This will improve existing methods and aid researchers in developing new methods to detect the presence of the toxin in laboratory and field samples.

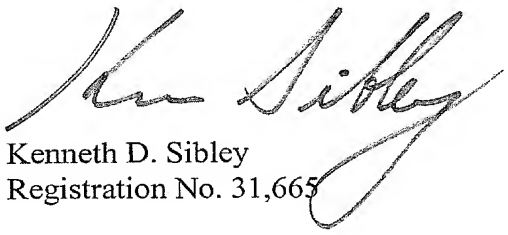
(C. Rubin et al., Emerging Areas of Research Reported during the CDC National Conference on *Pfiesteria*: From Biology to Public Health, *Environ Health Perspect* 109(suppl 5):633–637 (2001) (copy submitted concurrently herewith)). For all of the foregoing reasons, it is respectfully submitted that this rejection should be withdrawn.

Claims 14 stands rejected under 35 USC 103 as obvious over ***Moeller et al.*** in view of ***Larson et al.*** and ***Watanabe et al.*** applied above, and further in view of ***Glasgow et al.*** It is respectfully submitted that this rejection is obviated for the same reasons as set forth above, and respectfully submitted that this rejection should be withdrawn.

D. Conclusion.

In view of the foregoing, it is respectfully submitted that this application is in condition for allowance, which action is respectfully requested.

Respectfully submitted,



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Enclosure: C. Rubin et al. (2001)